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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,883	07/31/2003	Daniel Kahne	PUAM-0257	1801

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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER
CELSA, BENNETT M

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/631,883	KAHNE ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41,50-57,74-82 and 102-116* is/are pending in the application.

4a) Of the above claim(s) *39-41,50-57 and 74-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38 and 102-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/23/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-41, 50-57, 74-82 and 102-116 are currently pending.

Claims 39-41, 50-57 and 74-82 are withdrawn from consideration as being directed to a nonelected invention.

Claims 1-38 and 102-116 are under consideration.

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-38 and 102-116) in the correspondence dated 12/16/04 and Applicant's further election of glucose-C6 amine vancomycin with traverse is acknowledged. Applicant argues that it is not unduly burdensome to search and examine the entire application. This is not found persuasive for the reasons provided for in the restriction/election requirement (e.g. see pages 2-5) including reasons for patentable distinctness and search burden (e.g. different classification/bibliographic searches in patent/literature databases).

The requirement is still deemed proper and is therefore made FINAL.

Claims 39-41, 50-57 and 74-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

The elected species was not found; accordingly the search was extended to include other species within the scope of the generic claims (e.g. claim 1 and 102).

Specification/ Priority

The disclosure is objected to because of the following informalities: It is noted that the present application is labeled by applicant in the specification cross-refernece as a divisional application of 09/353,368 now US Pat. No. 6,710,168. However, the present application appears to be a continuation application since the elected invention in both applications was the same. Appropriate correction is required.

Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

1. Claims 1-38 and 102-116 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 1 (and dependent claims) the term (s) "modified alpha amino acid residue" lacks metes and bounds as to the modifications and resulting structure encompassed by the claimed invention.

B. In claim 1 (and dependent claims) the term “modified amino acid residue” as defined in multiple instances in the specification page 17 as including (e.g. comprising) “groups easily introduced” (e.g. substituents) is a relative term which renders the claim indefinite. The term "easily introduced " is not defined by the claim, and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

C. In claims 1, 2, 102, 103 (and dependent claims) the metes and bounds of "modified disaccharide" ("disaccharide modified to bear") regarding what chemical portion of the saccharide is being modified and (with respect to claim 1) which sugar residue(s) are being modified are indefinite.

D. Claim 1 (and dependent claims) is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are where (e.g what part of the modified/unmodified alpha amino acids; and what part of the glycosyl group) the "glycosidic bond" is formed between the peptide and glycosyl group (s) to form the glycopeptide.

E. Claim 1 (and dependent claims) is rejected since there is no metes and bounds regarding the upper limit (.e.g "one or more") of the "glycosidic groups" and "sugar residues" nor the chemical structure e.g. the metes and bounds of "glycosidic groups" and "sugar residues" within the scope of the presently claimed invention.

F. In claims 102, 107 (and dependent claims), the term "substituted amino group" lacks metes and bounds regarding the encompassed substituents and the ultimate structure.

G. In claim 102 (and dependent claims), the term "modified to bear at least one substituent which is not hydroxyl" lacks metes and bounds regarding the encompassed substituents and ultimate structure.

2. Claims 1-38 and 102-116 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vancomycin glucose C6 substituted derivatives of original claims 83-101 (and as described in specification table on pages 134-135), the specification does not reasonably provide enablement for the full scope of glycopeptides or glycopeptide antibiotics of claims 1 and 102 (and claims dependent thereon). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. .

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (USPQ 2d 1400: CAFC 1988) which include: a. The breadth of the claims.

b. The nature of the invention; c. The state of the prior art; d. The level of one of ordinary skill

e. The level of predictability in the art; f. The amount of direction provided by the inventor;

g. The presence or absence of working examples; h. The quantity of experimentation necessary needed to make or use the invention based on the disclosure; See :*In re Wands* USPQ 2d 1400 (CAFC 1988).

The breadth of the claims

The breadth of potential glycopeptides of different chemical structure as encompassed by claims 1 and 102 is huge in light of the failure to specifically claim the linkage and position between the peptide and glycoside portions of the glycopeptide as well as the failure to specifically claim the metes and bounds regarding the chemical

nature of the peptide (e.g. the nature of alpha amino acids and the position of the covalent bond) and glycoside portions as well as substituents therefrom for example as described in the indefinite rejection above:

A. In claim 1 (and dependent claims) the term (s) "modified alpha amino acid residue" lacks metes and bounds as to the modifications and resulting structure encompassed by the claimed invention.

B. in claim 1 (and dependent claims) the term "modified amino acid residue" as defined in multiple instances in the specification page 17 as including (e.g. comprising) "groups easily introduced" (e.g. substituents) is a relative term which renders the claim indefinite. The term "easily introduced " is not defined by the claim, and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

C.In claims 1, 2, 102, 103 (and dependent claims) the metes and bounds of "modified disaccharide" ("disaccharide modified to bear") regarding what chemical portion of the saccharide is being modified and (with respect to claim 1) which sugar residue(s) are being modified.

D. Claim 1 (and dependent claims) is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are where (e..g what part of the modified/unmodified alpha amino acids;

and what part of the glycosyl group) the "glycosidic bond" is formed between the peptide and glycosyl group (s) to form the glycopeptide.

E. Claim 1 (and dependent claims) is rejected since there is no metes and bounds regarding the upper limit (.e.g "one or more") of the "glycosidic groups" and "sugar residues" nor the chemical structure e.g. the metes and bounds of "glycosidic groups" and "sugar residues" within the scope of the presently claimed invention.

F. In claims 102, 107 (and dependent claims), the term "substituted amino group" lacks metes and bounds regarding the encompassed substituents and the ultimate structure.

G. In claim 102 (and dependent claims), the term "modified to bear at least one substituent which is not hydroxyl" lacks metes and bounds regarding the encompassed substituents and ultimate structure.

The nature of the Invention/State of the Prior art

The present invention is directed to the making and screening of glycopeptide antibiotics; although it is noted that claims 1 and 102 are not so limited. Additionally, it is noted that "the nature and placement of the sugars on the glycopeptide antibiotics play *critica*l roles in antibiotic activity" . In this regard it is further noted that, "that there have been no reports of modification on the glucose residues of vancomycin which have affected activity" E.g. see specification page 7, first full paragraph.

The level of one of ordinary skill

The level of one of ordinary skill in the art is masters or pHD level.

The level of predictability in the art

The sugar residues of the vancomycin and other glycopeptide antibiotics have been shown to affect binding activities e.g. "the nature and placement of the sugars on the glycopeptide antibiotics play *critica*l roles in antibiotic activity". Additionally, structural changes in the sugar residues can produce *significant* changes in antibiotic activity. See e.g. specification page 4, first full paragraph. Accordingly, the making and potential usefulness of "glycopeptide" compounds of different chemical structure is not *a priori* predictable. Courts have recognized that reaction steps *or compound structure* which is shown to be (e.g. by applicant or prior art) to be *critical or essential to the practice of the invention*, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); *Ex parte Bhide* (BdPatApp&Int) 42 USPQ2d 14.

The amount of direction/working examples

The specification only provides guidance and examples directed to the making and use (e.g. antibiotic) of vancomycin glucose C6 substituted derivatives of claims 83-101 which share a common structure which is not representative of the scope of claimed glycopeptides .

Quantity of Experimentation

In light of the unpredictability surrounding the making and use of glycopeptide derivatives of diverse structure which possess antibiotic activity, the undue breadth of the claimed invention, the lack of adequate guidance regarding the making and antibiotic testing of a representative sample of glycopeptides, the lack of metes and

bounds regarding claimed substituents, the lack of critical/essential core structure, one wishing to practice the presently claimed invitation would be unable to do so without engaging in undue experimentation.

3. Claims 1-38 and 102-116 are rejected under 35 U.S.C.112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (Lack of Written Description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in

University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The present invention is directed to the making and screening of glycopeptide antibiotics; although it is noted that claim 1 is not so limited. The breadth of potential glycopeptides of different chemical structure as encompassed by claims 1 and 102 (especially claim 1) is huge in light of the failure to specifically claim the linkage and position between the peptide and glycoside portions of the glycopeptide as well as the failure to specifically claim the metes and bounds regarding the chemical nature of the peptide (e.g. the nature of alpha amino acids and the position of the covalent bond) and glycoside portions as well as substituents therefrom; for example

A. In claim 1 (and dependent claims) the term (s) "modified alpha amino acid residue" lacks metes and bounds as to the modifications and resulting structure encompassed by the claimed invention.

B. in claim 1 (and dependent claims) the term “modified amino acid residue” as defined in multiple instances in the specification page 17 as including (e.g. comprising) “groups easily introduced” (e.g. substituents) is a relative term which renders the claim indefinite. The term "easily introduced " is not defined by the claim, and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

C. In claims 1, 2, 102, 103 (and dependent claims) the metes and bounds of “modified disaccharide” (“disaccharide modified to bear”) regarding what chemical portion of the

saccharide is being modified and (with respect to claim 1) which sugar residue(s) are being modified.

D. Claim 1 (and dependent claims) is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are where (e..g what part of the modified/unmodified alpha amino acids; and what part of the glycosyl group) the "glycosidic bond" is formed between the peptide and glycosyl group (s) to form the glycopeptide.

E. Claim 1 (and dependent claims) is rejected since there is no metes and bounds regarding the upper limit (.e.g "one or more") of the "glycosidic groups" and "sugar residues" nor the chemical structure e.g. the metes and bounds of "glycosidic groups" and "sugar residues" within the scope of the presently claimed invention.

F. In claims 102, 107 (and dependent claims), the term "substituted amino group" lacks metes and bounds regarding the encompassed substituents and the ultimate structure.

G. In claim 102 (and dependent claims), the term "modified to bear at least one substituent which is not hydroxyl" lacks metes and bounds regarding the encompassed substituents and ultimate structure.

Additionally, it is noted that "the nature and placement of the sugars on the glycopeptide antibiotics play *critica*l roles in antibiotic activity" .. Additionally, structural changes in the sugar residues can produce *significant* changes in antibiotic activity. See e.g. specification page 4, first full paragraph. Accordingly, the making and potential

usefulness of "glycopeptide" compounds of different chemical structure is not *a priori* predictable.

In support of such a broad genus, in an unpredictable art area, the specification only provides guidance and examples directed to the making and use (e.g. antibiotic) of vancomycin glucose C6 substituted derivatives of original claims 83-101 which share a common structure which is not representative of the scope of claimed glycopeptides . Such a narrow scope of examples fail to provide specification support for the claiming of such broad compound genera.

Claim Rejections - 35 USC § 102

4. Claims 1, 102 and 103 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Stack et al. EP 0802199A2 (10/22/97). Stack et al. disclose the compounds of formula I and II (see page 2) which are within the scope of the presently claimed invention as dalbaheptides containing a substituted disaccharide connected to the A4 peptide position. The reference compounds are within the scope of claim 1 since the proviso of claim 1 (e..g "provided that when A4 is linked to a disaccharide having a glucose residue that bears an N-substituted aminohexose residue, than said glucose residue is modified ... or P+R1R2R3") does not require that the modification occur on the glucose residue directly attached to A4. Similarly, the reference compounds are within the scope of claims 102-103 since these claims fail to identify the position of the disaccharide (e.g. first/second saccharide) groups relative to the peptide portion of the antibiotic.

5. Claims 1, 102 and 103 are rejected under 35 U.S.C. 102(e) as being anticipated by Cooper et al. US Pat. No. 5,843,889 (12/1998) . Cooper et al. disclose compounds within the scope of the presently claimed invention e.g. as dalbaheptides containing a substituted disaccharide connecting to an A4 peptide position. See e.g. formula I compounds (col.2) and the R substituents (e.g. R6 and R7 of col. 3-5); and the compounds of formula II, table 1 (col. 9-10) and specific compounds of table 2A (col. 14-15); and patent claims 1-9. The reference compounds are within the scope of claim 1 since the proviso of claim 1 (e..g "provided that when A4 is linked to a disaccharide having a glucose residue that bears an N-substituted aminohexose residue, than said glucose residue is modified ... or P+R1R2R3") does not require that the modification occur on the glucose residue directly attached to A4. Similarly, the reference compounds are within the scope of claims 102-103 since these claims fail to identify the position of the disaccharide (e.g. first/second saccharide) groups relative to the peptide portion of the antibiotic.

6. Claims 1-6, 9-15, 18-27 and 30-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Ge et al., Science Vol. 284 (April 16, 1999). See compounds 1-8, Fig. 2 and discussion therein.

7. Claims 1-38 and 102-116 are rejected under 35 U.S.C. 102(e) as being anticipated, or alternatively rendered obvious over Kahne, WO 00/42067 (7/00: provisional priority to 1/12/99. Kahne discloses glycopeptides comprising saccharides (e.g. modiified glucose containing disaccharides) linked via the A4 position to the peptide (preferably a dalbaheptide, including vancomycin analogs; with both generics and individual species (e.g. see examples; figures; claims) w/n the presently claimed invention. The reference generics

anticipate, or alternatively render obvious species within the scope of the presently claimed invention . E.g. see pages 2-3; claims.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-38 and 102-116 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-47 (especially claims 9 and 14 and claims dependent thereon) of U.S. Patent No. 6,498,238 (12/02). Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claim generic of compounds are within the scope of the presently claimed broader genus

(e.g. the patent claims dalbaheptapeptide derivatives which are vancomycin derivatives), as are the claimed patent species.

10. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Pat. No. 6,498,238, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

11. Claims 1-38 and 102-116 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,841,661 (1/05). Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claim generic of compounds are within the scope of the presently claimed broader genus (e.g. the patent claims dalbaheptapeptide derivatives which are vancomycin derivatives) as are the claimed patent species.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

11. Claims 1-38 and 102-116 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,710,168 (3/04). Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims teach compound species which are clearly within the scope of the presently claimed invention.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
March 8, 2005